and medium time disease remission, and that they often cause side effects. However, the list of incomplete or absent information is long. In particular we do not know:

Which is the best initial GC dose: If we can predict it in the individual patient (by gender, BMI, disease characteristics, etc.), the optimal glucocorticoid starting dosage is not defined yet, and varies widely across different studies, being comprised between 7 mg and 25 mg prednisone. The only controlled study suggests that initial prednisone doses <10 mg are associated with high incidence of recurrences at 2 months, whereas doses >20 mg are associated with considerable side effects. Some studies suggest that female gender and high ESR are indicators of the need of a higher initial dose, but these results have not been confirmed. A recent study supports the view that increased BMI is associated with poor response to GC, suggesting that its dosage should be adjusted to the patient’s weight. A multicentric study has been designed to compare two doses of prednisone, 20 mg and 12.5 mg.

If all GCs are the same: Prednisone, prednisolone, and methylprednisolone have not been directly compared for their efficacy in PMR. In spite of the initial promises, deflazacort seems not to have any advantage in terms of side effects, in particular osteoporosis, although its efficacy is similar to that of traditional GC.

How to taper GC: The intuitive reasoning behind rapid tapering is to reduce possible GC-related side effects. However, disease flares occur more frequently when a rapid dose reduction is used, although spontaneous disease flares can occur independently of GC dose. The general view is that 10 mg prednisone equivalent daily should be reached within 6–8 weeks, followed by tapering at a rate of about 1 mg/month. Shorter tapering schedules have been proposed, which permit to reduce prednisone from 12.5 mg daily to nil in 7 months. The baseline risk profile mentioned above should be taken into account when the tapering regimen is tailored. The main question is if rapid tapering, apart from the obvious disadvantage to the patient due to the increased number of relapses, corresponds to a lower cumulative dosage or not.

Duration of treatment: In one descriptive study, the initial dose was linked to treatment duration and cumulative dosage, for low initial doses were associated with low subsequent maintenance doses. PMR is probably more chronic than previously thought, with relapses occurring also years after successful treatment and GC interruption. However, it is not known if a longer treatment period is associated with less relapses at long-term follow-up. In view of the high incidence of GC-related side effects, which are associated with GC cumulative dosage, this attempt should be made to shorten as much as possible the course.

If there are effective alternative administration methods of GC: Intramuscular depot methyl prednisolone is effective in reducing the cumulative GC dosage and the incidence of vertebral fractures. In spite of this proved advantage, this route of administration has been not widely used.

12. A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY TO ASSESS THE EFFICACY AND SAFETY OF GEVKIZUMAB IN THE TREATMENT OF GIANT CELL ARTERITIS

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Background: GEVKIZUMAB—S78989—XOMA 052 is a recombinant human-engineered monoclonal antibody that binds and neutralizes human IL-1α when administered every 4 weeks by s.c. injection. There are ongoing trials in multiple inflammatory conditions. The rationale for IL-1 blockade as a therapeutic option in patients with GCA is as follows: IL1Ra KO mice develop large vessel vasculitis. In patients with GCA, IL1 is produced by the vessel wall infiltrate in a manner correlated with the intensity of the systemic inflammatory response and with corticosteroids requirements. IL-1 is also produced by the majority of activated circulating monocytes. IL-1 blocking therapy was shown to be effective in three patients with refractory GCA, yielding normalization of their inflammatory biomarkers and/or improvement in their symptoms.

Methods: The proposed study will be a randomized, double-blind, multicentre, placebo-controlled trial, with n = 50, 25 patients in each arm with a total duration of 12 months. The treatment arms will be Gevkizumab (60 mg s.c.) Q2W until week 4 then administered every 4 weeks for a total duration of 12 months. The treatment arms will be compared with placebo.

Target population: Male or female, age ≥50 years, weight >40 kg with previous GCA diagnosis according to the ACR 1990 criteria, with at least one previous relapse. The diagnosis should be confirmed either by a temporal artery biopsy or (in case of negative or absent TAB), or a positive imaging with either FDG-PET scan or CT angiogram. The patients should be on oral CS treatment no higher than 30 mg daily and have experienced a new GCA relapse limited to PMR-like or systemic symptoms.

Trial outcomes: Efficacy endpoints will be: proportion of responders to treatment at 4 weeks; proportion of patients in remission without CS after 6 months. Efficacy endpoints for renewed relapses for the 12 months period will be: proportion of patients in remission after 12 months; proportion of patients in relapse at 12 months; proportion of patients in remission after 24 months; proportion of patients in relapse at 24 months. The clinical outcomes will be the patient (PaGAA) and physician Global Assessment (PhGA) of disease activity; PMR activity score (PMR-AS); quality of life (SF-36); cumulative CS dose; inflammatory markers CRP and ESR. The safety endpoints will be adverse events, physical examination/vital signs, 12-lead ECG, laboratory safety parameters.

Trial organization: 9 countries are expected to be involved (incl. 3 countries outside EEA) with 20 centres in total. Regulatory authorities and EC approvals are currently being sought with expected first visit first patient in Q1 2014.